Citation:

Liese A, Schulz M, Fang F, Wolever T, D'Agostino R Jr, Sparks K, Mayer-Davis E. Dietary glycemic index and glycemic load, carbohydrate and fiber intake, and measures of insulin sensitivity, secretion and adiposity in the Insulin Resistance Atherosclerosis Study. *Diabetes Care.* 2005 Dec; 28 (12): 2,832-2,838.

PubMed ID: 16306541

Study Design:

Cross-sectional study

Class:

D - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To evaluate the association between digestible carbohydrates, fiber intake, glycemic index and glycemic load with insulin sensitivity (SI), fasting insulin, acute insulin response (AIR), disposition index, BMI and waist circumference in the Insulin Resistance Atherosclerosis Study (IRAS).

Inclusion Criteria:

- More than 1,600 participants were recruited at four clinical centers between 1992 and 1994 for the baseline IRAS exam
- Participants were recruited according to:
  - Glucose tolerance status (normal glucose tolerance, impaired glucose tolerance and non-insulin-taking type 2 diabetes)
  - Ethnicity (African American, Hispanic and non-Hispanic white)
  - Sex
  - Age (40-49 years, 50-59 years and 60-69 years).

Exclusion Criteria:

- Participants who did not meet above inclusion criteria during the initial Insulin Resistance Atherosclerosis Study (1992-1994)
- Individuals with diabetes at baseline were excluded because this may have altered their dietary behavior
- 16 participants were excluded due to missing data on glycemic index or glycemic load, 79 with missing values for SI, two with missing fasting insulin, four with missing anthropometric data and another six subjects with missing covariates. After model

diagnostics, one outlier was excluded. This left 979 participants with complete data for analysis.

Description of Study Protocol:

Recruitment

More than 1,600 participants were recruited at four clinical centers between 1992 and 1994 for the IRAS baseline exam. The goal was to obtain nearly equal representation of participants across:

- Glucose tolerance status (normal glucose tolerance, impaired glucose tolerance and non-insulin-taking type 2 diabetes)
- Ethnicity (African American, Hispanic and non-Hispanic white)
- Sex
- Age (40-49 years, 50-59 years, 60-69 years).

Design

Data on 979 adults with normal (67%) and impaired (33%) glucose tolerance from the Insulin Resistance Atherosclerosis Study (1992-1994) were analyzed.

Dietary Intake/Dietary Assessment Methodology

- Usual intake of diet was assessed by interview using a one-year, semiquantitative, 114-item food frequency interview modified from the National Cancer Institute Health History and Habits Questionnaire to include regional and ethnic food choices across the four clinical centers
- Participants were asked to recall intake of foods and beverages over the past year. Validity and reproducibility of the IRAS food-frequency questionnaire (FFQ) was demonstrated.

Blinding Used

Not applicable.

Intervention

Not applicable.

Statistical Analysis

- Analyses were limited to 1,087 individuals with normal (66%) or impaired (34%) glucose tolerance
- Multiple regression modeling was used
- All analyses were performed using SAS version 8.2 (SAS Institute, Cary, NC)
- To evaluate results in a manner comparable to previous work, the IRAS population was categorized into quintiles of carbohydrate intake, fiber intake, glycemic index and glycemic load and estimated mean levels of SI and adiposity within those categories
- The impact of potential effect modifiers, including age-groups, ethnicity, sex, family history of diabetes, BMI (in categories) and glucose tolerance status were evaluated by conducting stratified analyses and comparing the size and direction of the effect estimates
- Two-way interactions between exposures and effect-modifiers were examined
- The associations of carbohydrate-related exposures were first described at the unadjusted level and subsequently adjusted for confounders that were associated at the P 0.05 level

- The confounders in the most parsimonious models were age, sex, ethnicity/clinic, family history of diabetes, current smoking and total energy expenditure
- Education effects were not significant (NS), therefore this variable was omitted from final models
- To evaluate the contribution of demographic and lifestyle variables to the associations under study, this model was presented second
- In a third and final step, additional adjustment for total energy intake was made using the energy partition method, which controls for the non- carbohydrate contribution of correlated foods
- This approach was employed over other methods because in the categorical analyses, the ensuing categories retained information on amount of total dietary intake, allowing us to parse out the contribution of carbohydrates from non-carbohydrate sources such as protein and fat. This analysis was repeated using the residual method for energy adjustment to be able to compare the results directly with other studies.

Data Collection Summary:

Timing of Measurements

- IRAS required a two-visit protocol, the first to determine glucose tolerance status and the second to measure insulin sensitivity (SI). Participants were asked to fast for 12-hour before each of the two visits, abstain from heavy exercise and alcohol for 24 hours, and refrain from smoking the morning of the visit. A two-hour, 75 g oral glucose tolerance test was performed during the first visit, and World Health Organization criteria were used to assign glucose tolerance status
- Individuals currently taking oral hypoglycemic medications were classified as having type 2 diabetes regardless of the results of the oral glucose tolerance test (OGTT)
- SI and acute insulin response (AIR) were assessed using a 12-sample, insulin-enhanced, frequently sampled intravenous glucose tolerance test (FSI GT) with minimal model analysis.

Dependent Variables

- Insulin sensitivity: SI was calculated by mathematical modeling methods; the time course of plasma glucose was fit using non-linear least squares methods with the plasma insulin values as a known input to the system (according to the method known as MINMOD, which was developed by Richard N. Bergman, Ph.D., in 1986)
- Fasting insulin: Fasting plasma insulin was determined by radioimmunoassay
- Acute insulin response: AIR was calculated based on insulin levels through the eight-minute blood samples before insulin infusion
- Disposition index: Calculated as the product of AIR and SI
- BMI
- Waist circumference.

Independent Variables

- Glycemic index: Mean glycemic index values were assigned based on the white bread standard from published data and other available resources to all 114 FFQ line items plus three items assessed in the exam I interview on alcohol consumption (beer, wine, liquors) plus several additional foods (that were identified in open-ended questions as being consumed more than once per week)
- Average dietary glycemic index was computed by summing the products of the digestible

carbohydrate content per serving for each item, multiplied by the average number of servings of that food per day, multiplied by its glycemic index, all divided by the total amount of digestible carbohydrate daily intake. The average dietary glycemic load was computed like the glycemic index but by dividing by 100 instead of the total digestible carbohydrate intake. The average dietary glycemic index and glycemic load values were converted to the glucose 100 scale by multiplication with the factor 0.7.

Control Variables

None.

Description of Actual Data Sample:

- *Initial N:* 1, 087
- *Attrition (final N):* 979
- *Age:* 54.8±8.5 years
- *Ethnicity:*
  - Non-Hispanic white: 39.8
  - Hispanic: 34.2
  - African American: 26.0
- *Other relevant demographics:*
  - Current smoking: 16.2
  - Family history of diabetes: 39.6
- *Anthropometrics:*
  - BMI: 28.4±5.6
  - Waist circumference (cm): 90.6±12.8
- *Location:*
  - Columbia, South Carolina
  - Potsdam-Rehbruecke, Germany
  - Toronto, Canada
  - Winstom-Salem, North Carolina.

Summary of Results:

Key Findings

- No association was observed between glycemic index and AIR, disposition index, BMI or waist circumference after adjustment for demographic characteristics or family history of diabetes, energy expenditure and smoking
- Association observed for digestible carbohydrates and glycemic load, respectively, with adiposity were explained by energy intake
- In contrast, fiber was associated positively with SI and disposition index and inversely with fasting insulin, BMI and waist circumference, but not with AIR.

Author Conclusion:

- There was a lack of association of glycemic index, glycemic load and carbohydrate intake with measures of insulin sensitivity, insulin secretion and adiposity
- Consistent with previous findings, fiber intake was positively associated with SI and

inversely with adiposity and may additionally have a positive impact on pancreatic functionality.

Reviewer Comments:

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes
Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	N/A
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A

3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	Yes
4.	**Was method of handling withdrawals described?**	???
4.1.	Were follow-up methods described and the same for all groups?	???
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	???
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	Yes
5.	**Was blinding used to prevent introduction of bias?**	N/A
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	???
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes

6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	Yes
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	N/A
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A

8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	???
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes